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L2 and antibod$3	116

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DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=OR			
L3	L2 and antibod$3	116	L3
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L1	ubiquitin adj fusion adj protein	250	L1

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FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS, SCISEARCH, USPATFULL, PCTFULL'
ENTERED AT 15:17:19 ON 11 OCT 2005

L1 2272210 S UBIQUITIN(W)FUSION(W)PROTEIN? OR POLYPEPTIDE? OR PEPTIDE?
L2 6 S DIAGNOS? S ANTIBOD?
L3 439650 S ANTIBOD? AND L1
L4 129318 S L3 AND DIAGNOS?
L5 229019 S L1(S)ANTIBOD?
L6 6 S L1 AND L2
L7 516 S UBIQUITIN(W)FUSION(W)PROTEIN
L8 151145 S ANTIBOD?(S)DIAGNOS?
L9 129 S L7 AND L8
L10 129 DUP REM L9 (0 DUPLICATES REMOVED)
L11 28 S L9 AND 1960-1998/PY

1: Mol Immunol. 1997 Nov-Dec;34(16-17):1113-20.

Induction of cross-reactive antibodies against a self protein by immunization with a modified self protein containing a foreign T helper epitope.

Dalum I, Jensen MR, Gregorius K, Thomasen CM, Elsner HI, Mouritsen S.

M&E Biotech A/S, Horsholm, Denmark.

Self proteins are handled in the same way as foreign proteins by antigen presenting cells, but because of T-cell tolerance the presentation of self peptides does not normally lead to T cell activation. By providing physically linked T-cell help it is possible to overcome the B cell non-responsiveness toward self antigens. We have shown previously that a very potent antibody response, cross-reactive with a self protein, can be rapidly induced by immunizing with a recombinant immunogen consisting of the self protein with a foreign immunodominant T helper epitope inserted into its sequence (Dalum, I., Jensen, M. R., Hindersson, P., Elsner, H. I. and Mouritsen, S. (1996) J. Immnunol. 157, 4796). In this study we compare this approach for inducing autoantibodies against a self protein with the traditional method of conjugating the self antigen to a foreign carrier protein. The highly conserved self protein ubiquitin with an inserted epitope from ovalbumin (UbiOVA) is used as a model protein and compared to two traditionally conjugated immunogens consisting of ubiquitin chemically conjugated to a peptidic T helper epitope or to ovalbumin. The traditionally conjugated immunogens induce much slower and low titered ubiquitin specific antibody responses than the recombinant construct which also is capable of inducing antibodies directed against a much broader range of potential ubiquitin B cell determinants than the chemically conjugated immunogens. All three constructs are processed by antigen presenting cells and ovalbumin derived T cell epitopes are presented to T helper cells. From these observations it seems likely that the presence of non-shielded autologous B cell determinants on the immunogen is critical for the ability to induce a strong autoantibody response with a diverse fine specificity. Furthermore, the ubiquitin specific antibodies induced by UbiOVA contain higher levels of IgG2a/b relative to IgG1 compared to the conjugates. We therefore

speculate that the insertion of a T cell epitope directly into the self antigen could possibly induce an immune response with a different Th1/Th2 balance than a response induced with traditional conjugates.

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